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The Committee to Advise on Tropical Medicine and Travel (CATMAT)* and the National Advisory Committee on Immunization (NACI)**

TRAVEL, INFLUENZA, AND PREVENTION

Influenza infection causes fever, sore throat, muscle pains, cough, lassitude and headache. Annual attack rates average 10% to 20%, but may be higher during severe epidemics[1]. Malaise following influenza can persist for several weeks. Morbidity and mortality, associated with influenza, are usually more common in the older population[2] and in individuals with significant concurrent medical problems. These latter groups have been traditionally targetted for the immunization programs[3,4].

The 1918 panepidemic of influenza, estimated to have killed 20 million people worldwide, inflicted a major burden of disease and death on the young and previously healthy in Canada[5,6]. In the United States, it has been estimated that influenza causes millions of lost days from work[7] and 22,000 deaths per year[8]. A recent evaluation supports a more widespread administration of the influenza vaccine to produce "substantial health-related and economic benefits for healthy working adults"[9].

Influenza vaccination has not been recommended for people travelling abroad other than for those for whom it is normally recommended[3,4,10]. Travelling and travellers may represent an important combination of exposure to the virus and risk for influenza. In one study, "flu" symptoms were second only to gastrointestinal upset in passengers and crew on commercial air flights to the Russian Far East[11]. Although the rate of influenza symptoms in this study was no greater than for the general population in the U.S., the economic burden of disease due to disrupted travel, business and vacation plans would be at least as great as in the non-traveller.

The influenza season is usually from November to March in the northern hemispheres, and is reversed in the south (May to October). In the tropics, the virus can be isolated year around and epidemics of disease can occur at variable times of the year, including the summer months. The influenza vaccine is distributed early in the fall, usually in September, and is formulated annually based on new influenza strains predicted to arrive in Canada. Due to the reversed seasonality of influenza in the southern hemisphere, the North American formulated vaccine may not be a perfect match for those strains being transmitted in the south but will likely provide protection against some if not all of them. The vaccine is usually polyvalent. The 1996-1997 vaccine will be formulated to prevent three emerging influenza strains.

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As early as the 14th century plague panepidemic (1,348 in Venice, 1,377 in Rausa, and 1,383 in Marseilles), it was recognized that the transportation of people and goods was associated with the transmission of disease[12]. The early practice of "quarantine" (to hold for 40 days) was in response to this recognized threat, and eventually led to the adoption of the *International Sanitary Regulations* by the World Health Assembly in May 1951. In the last 45 years, significant changes in travel and transportation have occurred: more people are travelling, there are usually more individuals on a single conveyance, travel times are shorter, and distances travelled are greater, particularly by air. People are also travelling to more varied and exotic destinations.

The factors of population numbers and density, transportation speed and distance, combined with endemic disease risk and host susceptibility are creating new health-risk considerations for the traveller. Those considerations are the potential to acquire new or exotic diseases *while travelling* **and** the possibility to introduce new or exotic diseases to non-endemic areas *by travellers* (migrants).

Influenza outbreaks have been well described in relation to travel by train[13,14], aircraft[15], and ship[16,17]. An important aspect of influenza infection while travelling is the risk that the strain of the virus will not yet have been included in current vaccines. Therefore, vaccinated persons may not be fully protected[8]. Recommendations have been made to identify "high-risk" individuals who are proposing to travel abroad so that they and their eligible close contacts may be offered vaccination or post-influenza A exposure preventive therapy with amantadine or rimantadine[3,4,16,17]. Detailed guidelines and recommendations for the use of these agents for chemoprophylaxis and therapy are available[4].

Chemoprophylaxis is not a substitute for prevention by vaccination except when the vaccine is contraindicated or was not given prior to the onset of influenza A activity. Special target groups in this situation would be persons at high risk for morbidity or mortality from influenza A, persons providing care to those at high risk, persons who have immune deficiency and are expected to have an inadequate response to the vaccine, and other persons wishing to avoid influenza A illness for whom a decision on chemoprophylaxis should be made on an individual basis. This may be a therapeutic option for some travellers exposed to epidemic strains of influenza A, particularly on relatively slow moving long trips, such as may occur on some ships or train tours.

From a global and societal perspective, mathematical models for regional[10,18] and global[19] influenza epidemic spread have been described. These models are based on observations of influenza spread and assumptions of population migration and viral contagiousness. The European model of epidemic influenza spread indicates that, once introduced into a susceptible population, the time available for public health intervention is probably very short, possibly < 1 month, after the first detection of an epidemic influenza focus[20]. Such rapid spread would significantly limit the usefulness of immunization as a preventive measure.

The ability of vaccination to prevent or delay the introduction of influenza on a large-scale population basis has not been demonstrated in prospective studies. The mass movement of people within and between countries would make such a study difficult to do. Several studies have demonstrated herd immunity following influenza vaccination[21-24]. Most of these studies have been done in relatively small and closed environments such as nursing homes. One study suggested that immunization increased herd immunity against influenza on a state-wide basis[24].

Summary

There are three possible objectives to immunize for influenza: 1) protection of the health of the individual; 2) prevention of outbreaks; and 3) prevention of spread from one region to another.

Given the demonstrated benefits of influenza vaccination for high-risk individuals[2,4-8], relatively cloistered populations[21-23], and now the healthy, young population[9]; the observed individual risks of acquiring influenza associated with mass transportation[13-17]; and the potential role of rapid transportation in the spread of influenza[18-20], the following recommendations for the prevention of influenza related to travel are made.

Recommendations

1. Routine, primary immunization against influenza, for the susceptible general population, should follow the annual recommendations of NACI[3,25] based on the predictions for endemic and epidemic influenza strains. These recommendations are made independently of the intention to travel. The directions for the use of the vaccine, with particular attention to contraindications and vaccine-associated adverse events, should also follow the general influenza vaccination recommendations of NACI[3].

   Evidence-based medicine category[26]: Good evidence to support a recommendation for use. Evidence from at least one properly designed randomized, controlled study. (AI)

2. Pre-departure influenza immunization for prevention of the disease in travellers should be considered for anyone leaving Canada during the local influenza transmission season.

   Evidence-based medicine category: Moderate evidence to support a recommendation for use. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies, preferrably from more than one centre, from multiple time series, or from dramatic results in uncontrolled experiments. (BII)

3a. Pre-departure influenza immunization* for prevention of the disease in travellers should be offered to anyone leaving Canada who will be exposed during the influenza transmission season **at the destination****. This may also reduce or delay the risk of introducing influenza into Canada upon returning home. This will require that a special effort is made by primary care givers and travel medicine providers to stock influenza vaccine outside of the fall months when it is usually used in Canada.

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* If the available influenza vaccine in Canada does not include the strains of virus being transmitted where and when the traveller will be at risk, obtaining the appropriate vaccine, if available and if it can be safely administered, should be considered at the destination.

** **NOTE:** Influenza transmission seasons vary around the world. Check with the local Medical Officer of Health or other Public Health source (WHO, LCDC FaxLink (613) 941-3900) for influenza activity and transmission seasons globally.

Evidence-based medicine category: Moderate evidence to support a recommendation for use. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies, preferably from more than one centre, from multiple time series, or from dramatic results in uncontrolled experiments. (BII)

3b. To reduce the risk of influenza in the individual, Canadians who are abroad and will be returning to Canada from an influenza transmission zone, and who were not or could not be vaccinated against the disease before leaving Canada, **should consider being vaccinated during their stay at their destination, and before returning to Canada.** This intervention may also reduce or delay the risk of introducing influenza into Canada on their return.

Evidence-based medicine category: Moderate evidence to support a recommendation for use. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies, preferrably from more than one centre, from multiple time series, or from dramatic results in uncontrolled experiments. (BII)

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International Notes

PROGRESS TOWARDS THE ELIMINATION OF LEPROSY AS A PUBLIC HEALTH PROBLEM

Introduction

For the first time since global statistics on leprosy were collected, the number of patients registered for treatment in the world has fallen below 1 million. More importantly, almost all registered cases now have access to multidrug therapy (MDT). Improvements in the coverage of leprosy elimination programs have led, in turn, to improved case detection and also to a steady increase in coverage with MDT from 76% to 91% in the last year. Thus, the large backlog of leprosy patients waiting for appropriate treatment has been reduced significantly and the gap between the number of estimated cases and the number of cases registered for treatment is steadily decreasing. However, it should be recognized that, in some countries, substantial numbers of patients do not have easy access to diagnosis and treatment; this could hamper the elimination of leprosy at the national and subnational levels in a number of highly endemic countries.

The prevalence of leprosy worldwide was reduced by 28% between 1995 and 1996, compared with 27% between 1994 and 1995. These reductions can be explained by the conjunction of the following factors: wider implementation of MDT; fixed duration of treatment; and updating of the leprosy registers.

Table 1
Registered cases of leprosy and coverage with multidrug therapy (MDT), by WHO region, 1996

WHO Region	Registered cases	Prevalence per 10,000	Cases on MDT	MDT coverage (%)	Cured with MDT (cumulative total)
Africa	95,901	1.77	87,739	91.5	443,610
Americas	123,537	1.64	93,004	75.3	225,450
South-East Asia	651,562	4.72	610,669	93.7	7,059,925
Eastern Mediterranean	23,005	0.54	19,083	83.0	52,784
Western Pacific	32,254	0.20	31,943	99.0	206,635
TOTAL	**926,259**	**1.67**	**842,438**	**91.0**	**7,988,404**

Estimated prevalence

In the absence of precise tools to measure infection, and considering that the diagnosis of leprosy is mainly clinical, it is somewhat difficult to estimate the true prevalence of leprosy in the world. Estimates presented in this report are based on information provided by national program managers and are derived from registered figures, taking into account health service coverage and MDT implementation. Despite limitations, global estimates are believed to be accurate enough for priority setting and for planning intensified activities at the national and subnational levels.

Estimates for 1996 indicate that there are about 1.3 million cases of leprosy in the world. It is estimated, however, that over 330,000 leprosy cases have yet to be detected, about 50% of them living in Asia. The widest gaps between registered and estimated cases are reported particularly in countries with poor service coverage.

Registered prevalence

There was a significant reduction in the number of registered cases worldwide (-28%) from 1995 (1,286,932 cases) to 1996 (926,259 cases); this reduction has been observed in all endemic countries and regions, with the exception of Guinea, Sudan and Madagascar. Over the past 10 years, the leprosy problem was reduced by 83% worldwide, although the reduction in the American Region was only 60%.

The global prevalence rate of registered cases decreased from 2.3 to 1.7 per 10,000 population between 1995 and 1996. However, in the top 16 endemic countries, the prevalence rate is still 4.5 per 10,000, i.e., 5 times higher than the elimination target (below 1 case per 10,000 population).

Detection of leprosy cases

Since 1993, the global detection of leprosy cases has declined, although it is difficult to interpret this trend. Declines have been observed in all WHO Regions, with the exception of the Americas.

Annual detection rates are still very high in some countries, or in some regions within countries. The extent to which this reflects the high level of disease transmission is not clear, but these countries or regions will have significant difficulty in reaching the elimination target on time and will need special attention.

Achievements with MDT

By the beginning of 1996, more than 90% of registered leprosy patients were being treated with MDT and, so far, about 8 million persons have been cured through this treatment. During 1995, more than 1.5 million cases, old and new, received MDT. Table 1 gives details of MDT coverage for registered patients at the global and regional levels.

Clearly, this illustrates the important progress made in a span of 2 years, i.e. an MDT coverage of 91% in 1996 compared with 55% in 1994. The increase in MDT coverage is a result of the efficacy and acceptability of MDT which is fully standardized and of fixed duration. The number of treatment failures or relapses remains very low and drug resistance to MDT has never been reported. The supply of adequate quantities of drugs at the peripheral level, together with the fact that treatment is free of charge, have contributed to optimal compliance.

Progress towards the elimination of leprosy

Leprosy remains a public health problem in 60 countries or areas, but 16 countries account for 90% of the leprosy problem in the world.

Conclusion

The strategy for eliminating leprosy as a public health problem has already had a significant impact: the dramatic and constant reduction in morbidity; increased priority to leprosy control activities in the most endemic countries; free supply of MDT drugs through WHO to the countries in need; and focused attention on difficult-to-reach populations. These are some of the direct benefits of this strategy, although these encouraging achievements should not undermine the fact that considerable challenges still remain before the elimination of leprosy in some parts of the world can be attained.

Source: *WHO Weekly Epidemiological Record, Vol 71, No 20, 1996.*

ADVISORY NOTICE: INFECTION CONTROL FOR CREUTZFELDT-JAKOB DISEASE

The Division of Nosocomial and Occupational Infections and the Division of Blood-borne Pathogens, Bureau of Infectious Diseases, LCDC, has received enquiries related to updated infection control (IC) methods for patients with Creutzfeldt-Jakob Disease (CJD). The 1992 Health Canada *Infection Control Guidelines: Isolation and Precaution Techniques* provide some recommendations. These Guidelines are currently being revised, including the recommendations for CJD. Other jurisdictions and organizations have published IC guidelines for CJD[1-6] and these provide pertinent information.

Human infection with the CJD agent is known to occur. All cases have resulted from either direct exposure of the brain to the CJD agent (e.g., dura mater graft) or peripheral injection of a CJD agent-contaminated product derived from human brain (pituitary hormone).

Cases of CJD have been reported in health care workers, but there is no epidemiologic evidence to indicate that health care workers are at increased occupational risk for CJD. However, practices to minimize the exposure of health care workers should be in place.

Special CJD-specific IC precautions are recommended for patients who have, are suspected of having, or are at substantially increased risk of developing CJD [i.e., persons who have received human pituitary hormone (growth hormone and gonadotrophin) or dura mater grafts or members of a family where CJD is recognized as being familial].

There is no human evidence of CJD transmission from patients who are asymptomatic for CJD and not at increased risk of developing CJD (as defined in the previous paragraph). Therefore, such patients do not need special CJD-specific IC precautions.

The clinical diagnosis of CJD can be difficult, especially in the early clinical phase or if the presentation is atypical. It is problematic as to what IC practices should be recommended for patients who have undiagnosed neurologic illness, especially dementing illness. Credible guidelines from other jurisdictions are not consistent. The United Kingdom guidelines[1] do not consider these patients to be a risk group that needs special CJD-specific IC precautions. Australian guidelines[2] classify any patient with undiagnosed progressive neurologic illness with or without dementia as at increased but not high risk for having CJD and some special CJD-specific IC precautions are recommended. LCDC, in consultation with external advisors, is examining this issue in detail.

Health care organizations or professionals needing to discuss IC precautions for CJD may contact LCDC staff at 613-952-9875.

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Source: *Blood-borne Pathogens Division and Nosocomial and Occupational Infections Division, Bureau of Infectious Diseases, LCDC, Ottawa.*

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